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09/489,711	01/24/2000	David S. Roberts	PC10299A	6167

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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/489,711	ROBERTS ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,26,27,30-32,40 and 41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17, 26, 27, 30-32, 40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

1) Acknowledgment is made of Applicants' amendment filed 02/23/06 in response to the non-final Office Action mailed 08/24/05.

Status of Claims

2) Claims 13, 16, 24, 25 and 33 have been canceled via the amendment filed 02/23/06.

Claims 17, 27, 30 and 31 have been amended via the amendment filed 02/23/06.

New claims 40 and 41 have been added via the amendment filed 02/23/06.

Claims 17, 26, 27, 30-32, 40 and 41 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claim 33 made in paragraph 9 of the Office Action mailed 04/16/05 and maintained in paragraph 23 of the Office Action mailed 08/24/05 under 35 U.S.C § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

6) The rejection of claim 33 made in paragraph 25 of the Office Action mailed 08/24/05 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is moot in light of Applicants' cancellation of the claim.

7) The rejection of claim 25 made in paragraph 26(b) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 33 made in paragraph 26(f) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicants'

cancellation of the claim.

9) The rejection of claims 24, 25 and 33 made in paragraph 27 of the Office Action mailed 08/24/05 under 35 U.S.C § 102(b) as being anticipated by Frantz *et al.* (US 5,695,769- already of record) as evidenced by Barenholz *et al.* (US 6,156,337 - already of record) and Zarkasie *et al.* (*J. Vet. Med. Sci.* 58: 87-89, 1996, already of record), is moot in light of Applicants' cancellation of the claims.

10) The rejection of claims 13 and 16 made in paragraph 28 of the Office Action mailed 04/16/05 under 35 U.S.C § 103(a) as being unpatentable over Frantz *et al.* (US 5,695,769- already of record) in view of Applicants' admitted state of the prior art, and Barenholz *et al.* (US 6,156,337 - already of record), is moot in light of Applicants' cancellation of the claims.

Rejection(s) Withdrawn

11) The rejection of claims 17, 30 and those dependent therefrom, made in paragraph 9 of the Office Action mailed 04/16/05 and maintained in paragraph 23 of the Office Action mailed 08/24/05 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendments to the claims.

12) The rejection of claims 17, 30 and those dependent therefrom made in paragraph 25 of the Office Action mailed 08/24/05 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' arguments.

13) The rejection of claim 31 made in paragraph 26(a) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claim 27 made in paragraph 26(c) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

15) The rejection of claim 30 made in paragraphs 26(d) and 26(e) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

16) The rejection of claims 31 and 32 made in paragraph 26(f) of the Office Action mailed 08/24/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of

Applicants' amendment to the base claim.

17) The rejection of claims 17, 26, 27 and 30-32 made in paragraph 27 of the Office Action mailed 08/24/05 under 35 U.S.C § 102(b) as being anticipated by Frantz *et al.* (US 5,695,769- already of record) as evidenced by Barenholz *et al.* (US 6,156,337 - already of record) and Zarkasie *et al.* (*J. Vet. Med. Sci.* 58: 87-89, 1996, already of record), is withdrawn in light of Applicants' amendment to the claims and/or the base claim(s).

New Rejection(s) Based on Applicants' Amendment

The new rejections set forth below are necessitated by Applicants' amendments and/or the submission of new claims.

Rejection(s) under 35 U.S.C § 112, First Paragraph (New Matter)

18) Claim 31 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 31, as amended, depends from claim 17 or claim 30. The vaccine composition of claim 31 as dependent from claim 17 therefore comprises an antigen composition comprising a fluid fraction of an *Erysipelothrix rhusiopathiae* culture that is inactivated with beta-propiolactone (BPL) and is substantially free of cells of *Erysipelothrix rhusiopathiae*, a stabilizing agent which is a metal hydroxide, a metal phosphate, an aluminum hydroxide gel, a calcium phosphate gel, a zinc hydroxide/calcium hydroxide gel or an alum, and an adjuvant composition comprising about 2% v/v lecithin, about 18% v/v mineral oil, and a combined volume of about 8% v/v of Tween 80 and Span 80 surfactants with the remaining volume being saline solution, wherein said composition is stable at 2°C to 8°C for at least one year and protects weaned pigs against *Erysipelothrix rhusiopathiae* infection for six months. In other words, the vaccine claimed in claim 31 is required to comprise a fluid fraction of an *Erysipelothrix rhusiopathiae* culture that is inactivated with beta-propiolactone (BPL) and that is substantially free of cells of *Erysipelothrix rhusiopathiae* plus a generic 'metal phosphate' or 'metal hydroxide', or 'a calcium phosphate gel', or 'a zinc hydroxide/calcium hydroxide gel or an alum', or 'an aluminum hydroxide gel', and an adjuvant composition comprising about 2% v/v lecithin, about 18% v/v mineral oil, and a combined volume of about 8% v/v of Tween 80 and Span 80 surfactants with

the remaining volume being saline solution, and is required to be stable at 2°C to 8°C for at least one year, and is required to protect weaned pigs against *Erysipelothrix rhusiopathiae* infection for six months. However, there is no descriptive support within the instant specification for such a vaccine composition comprising the recited antigen composition, the recited adjuvant, and the generically recited stabilizing agent which is a 'metal phosphate' or 'metal hydroxide', or 'a calcium phosphate gel', or 'a zinc hydroxide/calcium hydroxide gel or an alum, or 'an aluminum hydroxide gel' of any concentration other than an aluminum hydroxide gel that is present at a concentration of about 30% v/v. The only vaccine composition that protected weaned 3 week-old pigs against *E. rhusiopathiae* for six months is the vaccine composition that was stored at 4°C for 12 months and that contained about 10X concentrated culture filtrate antigen of *E. rhusiopathiae* from a formalin- or BPL-inactivated culture of *E. rhusiopathiae* and combined with about 30% v/v REHYDRAGEL stabilizing agent, and an adjuvant comprising 10% lecithin in DRAKEOL™ mineral oil, 5.6% Tween 80 and 2.4% Span 80 in PBS. See Examples 4, 3 and 2; and pages 12-15. Therefore, the above-identified limitations in the instant claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the above-identified limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C § 112, Second Paragraph

18) Claims 17, 26, 27, 30-32, 40 and 41 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 32 is vague, indefinite and confusing in the limitation 'Claim 17 or 30, wherein said *E. rhusiopathiae* culture is inactivated with formalin'. Claim 32 depends from claim 17 or claim 30, which claim recites that 'the *E. rhusiopathiae* culture is inactivated with beta-propiolactone'. Is the *E. rhusiopathiae* culture recited in the dependent claim 32 inactivated for the second time with formalin?

(b) New claim 40 is vague, indefinite, incorrect and/or has improper antecedent basis in the limitation: 'The antigen composition of Claim 17', because claim 17 is drawn to 'A vaccine composition', but not to 'An antigen composition'.

(c) New claim 41 is vague, indefinite and incorrect in the limitation: 'The vaccine composition of Claim 40', because as presented currently, claim 40 is drawn to 'The antigen composition' as opposed to --The vaccine composition--.

(d) Claim 27, as amended, is vague and lacks proper antecedent basis in the limitation: 'the concentrated composition'. Claim 27 depends indirectly from claim 40, which recites 'a concentrated antigen composition'. For proper antecedence, it is suggested that Applicants replace the limitation with --the concentrated antigen composition--.

(e) Claims 17 and 30 contain the trademark/trade names 'Tween 80' and 'Span 80'. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982)*. The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade names are used to identify/describe 'Tween 80' and 'Span 80' and, accordingly, the identification/description is indefinite.

(f) Claims 26, 27, 30-32, 40 and 41, which depend from claim 17 or 30, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 103

19) Claims 17, 26, 27, 30-32, 40 and 41 are rejected under 35 U.S.C § 103(a) as being unpatentable over Frantz *et al.* (US 5,695,769 - already of record) in view of Applicants' admitted state of the prior art, Zarkasie *et al.* (*J. Vet. Med. Sci.* 58: 87-89, 1996, already of record) and Barenholz *et al.* (US 6,156,337 - already of record).

The term 'about' with regard to the v/v concentration of the stabilizing agent, or the adjuvant ingredients recited in the instant claims, is interpreted in this rejection as encompassing

$\pm$ 10.

Frantz *et al.* disclosed a vaccine composition comprising a culture fluid fraction obtained from an inactivated culture of *Erysipelothrix rhusiopathiae*. The fraction is clarified by centrifugation and therefore is substantially free of cells of *Erysipelothrix rhusiopathiae*. The fluid antigen fraction is then concentrated by ultrafiltration to a calculated OD of 16.67. See sections 'B. Inactivation of Bacteria' and 'C. Vaccine Fluid Preparation' in the upper half of column 17. The antigen composition further comprises an aluminum hydroxide gel carrier, i.e., REHYDRAGEL or REHYDRAGEL HPA, or calcium phosphate, or alum at a concentration of between 15 and 60% (see lines 55-65 in column 6; paragraph bridging columns 6 and 7; and the first full paragraph in column 7) and a saponin adjuvant (see claim 7; and lines 41-43 in column 5). The antigen composition comprises saline, DRAKEOL, i.e., lecithin and mineral oil emulsion at various concentrations, and between 0.7% to 3.2% Tween 80 and 0.3% to 1.8% Span. The lecithin and mineral oil emulsion is present at a concentration of 5 to 40%, or 10% (see claims and second full paragraph in column 21), or combined 4% v/v of Tween 80 and Span 80 (see the Table in column 19). The *Erysipelothrix rhusiopathiae* antigen-containing vaccine induced the best immunity in swine (see Example 11). Frantz's vaccine composition claimed in Frantz's claim 3 and used in Frantz's method of claim 10 represents a vaccine composition that comprises the vaccine described in Example 9 of the Frantz patent. The vaccine composition described in Example 9 comprises 5% oil/lecithin and a combined volume of 4% (i.e., 4 $\pm$ 10) v/v of Tween 80 and Span 80, saline, and aluminum hydroxide gel. The *Erysipelothrix rhusiopathiae* bacterin present therein is produced as described in Example 7. Example 7 describes a formalin-inactivated *Erysipelothrix rhusiopathiae* containing aluminum hydroxide to a final concentration of 25%, i.e., 25 $\pm$ 10.

Frantz *et al.* do not expressly teach that the *Erysipelothrix rhusiopathiae* is inactivated by betapropiolactone (BPL).

However, Frantz *et al.* expressly taught that other inactivating agents, such as, BPL or betapropiolactone may be used as an inactivating agent alternative to formalin or formaldehyde solution (see the first full paragraph in column 6).

Given the art-known use of betapropiolactone as an inactivating agent alternative to formalin or formaldehyde, it would have been *prima facie* obvious to one of ordinary skill in the

art at the time the invention was made to use betapropiolactone as the inactivating agent in place of formalin to inactivate Frantz's *Erysipelothrix rhusiopathiae* culture to produce the vaccine composition of the instant invention with a reasonable expectation of success. The instant specification acknowledges the following to be known in the art: the use of inactivating agents 'known in the art', for example, formalin (formaldehyde), beta propiolactone, or other chemical agents having properties similar to these agents. See lines 17-19 on page 4 of the instant specification. Thus, not only Frantz *et al.* expressly suggested the use of beta-propiolactone as an alternative inactivating agent to inactivate the bacterial culture, but Applicants' admitted state of the prior art also acknowledges BPL to be an art-known inactivating agent alternative to formalin (formaldehyde). Given that the use of BPL as a bacterial inactivating agent is not critical for the instant invention as is evident from the description at lines 17-19 on page 4 of Applicants' specification, the substitution of one inactivating agent with another, admittedly art-known, alternative inactivating agent was well within the realm of routine experimentation, would have been obvious to one of ordinary skill in the art, and would have brought about similar results or effects. In the instant invention, the BPL-inactivated culture did not show any unexpectedly more effective protection in pigs compared to the formalin-inactivated cultures. See the sentence bridging pages 11 and 12 of the instant specification. That aluminum hydroxide in Frantz's composition intrinsically served as a stabilizing agent is implicit from the teachings of Frantz *et al.* in light of what was known in the art. For instance, Barenholz *et al.* taught the dual role of aluminum hydroxide both as an adjuvant and as a stabilizer in microbial vaccines (see column 13, last two lines). The ability to protect an animal or weaned pigs against *Erysipelothrix rhusiopathiae* is viewed as an uncharacterized functional property inseparable from the prior art vaccine composition in light of what was well known in the art. For instance, Zarkasie *et al.* expressly taught that protective antigens of *Erysipelothrix rhusiopathiae* are abundant in the culture filtrate (see page 89, right column), or rich in culture supernatant (see page 90, left column). Although Frantz *et al.* are silent about the stability of the composition at 2°C to 8°C for at least one year and about the conferring of protection to weaned pigs for six months, these properties not expressly recited by the Frantz patent, are viewed as uncharacterized functions of the prior art composition inseparable from said composition.

With regard to the recited specific v/v concentration of lecithin, mineral oil, or 30% aluminum hydroxide gel as recited in the instant claims, the optimization of the v/v concentration to the specific concentration as recited, is well within the realm of routine experimentation. It has been held legally obvious and within the routine skill in the art to optimize result-effected variables. The v/v concentration of lecithin, mineral oil, or the 30% v/v aluminum hydroxide gel concentration as recited is clearly a result-effected variable, and it would have been obvious to one of ordinary skill in the art at the time of the invention to vary or optimize the v/v concentration of lecithin, mineral oil, or 30% aluminum hydroxide gel in Frantz's vaccine composition as modified by Zarkasie *et al.*, Barenholz *et al.* and Applicants' admitted state of the prior art by routine experimentation to produce the instant invention.

Claims 17, 26, 27, 30-32, 40 and 41 are *prima facie* obvious over the prior art of record.

Remarks

20) Claims 17, 26, 27, 30-32, 40 and 41 stand rejected.

21) Applicants' amendments necessitated the new ground(s) of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

22) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The central Fax number for submission of amendments, responses or papers is (571) 273-8300.

23) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

24) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

March, 2006

S. DEVI, PH.D.
PRIMARY EXAMINER